

# Optical coherence tomography for non-invasive diagnosis of basal cell carcinoma

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# CHAPTER 7

**Impact paragraph**

## RESEARCH

This thesis focused on the (cost-)effectiveness of optical coherence tomography (OCT)-guided diagnosis and treatment of skin lesions clinically suspected for basal cell carcinoma (BCC) compared to regular care punch biopsy. We provided insight in patient preferences and investigated the potential of using OCT in alternative subgroups of patients. In addition, we searched for ways to improve the interpretation of OCT scans by investigators.

## SCIENTIFIC IMPACT AND RESULTS

Basal cell carcinoma (BCC) is the most common form of skin cancer. Nowadays, one in five to six people in the Netherlands will develop a BCC during their lifetime.<sup>1-3</sup> Sometimes BCC diagnosis is evident based on the clinical appearance, but most often a punch biopsy is performed under local anaesthesia to verify the clinical diagnosis and to determine the BCC subtype.<sup>4,5</sup> A punch biopsy is a small invasive procedure. The injection of the anaesthetic can be painful and there is a small chance of complications (bleeding, infection and scar formation). Awaiting the results takes approximately one to two weeks, after which the results are discussed with the patient in a (telephone) consultation. This causes treatment delay and the uncertainty during this period may be stressful for patients. In this thesis we investigated whether in part of the patients who visit the outpatient dermatology clinic with a skin lesion suspected for BCC, an accurate non-invasive diagnosis can be made with OCT. Hence, in part of the patients, BCC diagnosis and treatment can be accomplished in one day. Implementation of OCT into clinical practice is thus expected to lead to a more efficient, patient friendly and potentially cost-saving healthcare.

As large, well-conducted randomised controlled trials were lacking, it was unclear whether a diagnostic strategy using OCT for diagnosis and treatment does not result in an unacceptable increase in treatment failure (residual or recurrent (pre-) malignant skin lesion) when compared to regular care using punch biopsy in the large majority of patients. Therefore, we conducted the first randomised controlled non-inferiority trial (the ROCTI-trial) in which we compared the 1-year probability of treatment failure of an OCT-guided diagnosis and treatment to regular care punch biopsy. Costs of both strategies were also compared and to get a good impression of the perspective from patients their preferences were explored. In order to make the results generalizable, the trial was conducted in three hospitals: two general hospitals and one academic hospital.

We showed that OCT-guided diagnosis and treatment is non-inferior compared to regular care. It leads to more efficient healthcare since almost two-third of

biopsies (65.6%) could be omitted. OCT is also a cost-effective strategy compared to regular care punch biopsy. Patient preferences show that OCT is accepted by patients in clinical practice. As the ROCTI-trial was only performed in patients with an indication for biopsy, the results were not entirely generalizable for all BCC patients. Therefore, we also evaluated the added value of OCT in patients in whom there was no indication for a biopsy, namely patients with clinically evident BCCs that are immediately surgically removed without prior biopsy. These patients were not included in the ROCTI-trial, but it is possible that a skin lesion which is actually not a BCC, is incorrectly diagnosed as BCC by the clinician. We found that OCT was able to slightly reduce the risk of incorrect diagnosis by clinicians of non-BCC lesions as BCC. However, the risk of incorrect BCC diagnosis by clinicians is already very low and the value of OCT thus seems limited.

Apart from using OCT for diagnosis of BCC, we explored the application of OCT in alternative subgroups of patients. As such, we evaluated if OCT was helpful for determining the resection margins of BCC prior to Mohs micrographic surgery (MMS), a specialised surgical method. This method is performed in stages by removing the tumour together with a thin (1-2mm) layer of surrounding normal tissue. As MMS is a labour-intensive and time-consuming procedure, correct estimation of resection margins with OCT prior to MMS could reduce the average number of stages required for complete tumour removal. Unfortunately, OCT was not accurate when used for this purpose and we also found that obtaining and interpreting the OCT scans was time consuming.

Besides looking in which subgroups of patients OCT can be applied, we searched for ways to improve the interpretation of the OCT scans by the investigator. During the assessment of OCT scans, the investigator tries to identify features that are typical for BCC. We conducted a study in which we evaluated which features are most discriminative for BCC, as using only a small set of features can ease the interpretation of OCT scans by the investigator.

Finally, we investigated whether we could improve the quality of the OCT scan in order to facilitate correct diagnosis. We tried to improve OCT image quality and thereby visibility of BCC features by application of glycerol on the skin, a so-called optical clearing agent. We found that although application of glycerol on the skin increased the optical penetration depth, it did not have a clinically relevant effect and therefore was not recommended.

Lastly, the level of experience of the investigators who interprets OCT scans may influence their ability to make both accurate and confident diagnoses with OCT. We showed that for novice OCT assessors, distant supervision from an OCT expert who is not on-site and has no clinical information, is still valuable.

The ROCTI-trial generated the necessary high-level evidence for implementation of OCT in clinical practice. The other studies in this thesis contributed knowledge about the applicability of OCT in alternative subgroups of patients, as well as ways to improve the interpretation of OCT scans.

## **SOCIETAL IMPACT**

In the Netherlands, approximately 50.000 patients were diagnosed with a new BCC in 2021. About one-third of these patients were or will be diagnosed with more than one BCC. The number of biopsies that are performed in patients with a skin lesion clinically suspected for BCC, is much higher and approximately 90.000 each year. These numbers continue to rise, illustrating that BCC is a public health problem that puts a substantial burden on the resources of healthcare systems, as well as a heavy economic burden on society, being associated with significant direct medical costs.

We found that with OCT, almost two-third (65.6%) of biopsies are no longer needed. The results of this thesis are relevant for patients who visit the dermatology outpatient clinic with a lesion suspected for BCC for which a biopsy needs to be taken. An invasive procedure can be omitted and treatment can often be discussed and started immediately. For clinicians, use of OCT is relevant because it can decrease the workload caused by the high number of biopsies and post-biopsy (telephone) consultations. And from a healthcare perspective the results are also of interest given their aim to make the diagnostic process more efficient, patient friendly and less costly.

## **RECOMMENDATIONS FOR IMPLEMENTATION**

The research presented in this thesis lays the foundation for implementation of OCT in clinical practice.

To facilitate successful implementation of OCT in clinical practice, (inter) national dissemination and implementation activities will need to be conducted. Dissemination activities are of high importance to create awareness within the dermatological community and among patients. A summary of the most important results of the ROCTI-trial can be accessed by patients on the website of ZonMw. Relevant patient associations (Huidpatiënten Nederland) can be involved in the development of dedicated patient information folders and information videos about OCT. To increase awareness of the results among the dermatological community, we presented and discussed the results of the studies on national and international (scientific) meetings.

The results of the studies in this thesis have been published in scientific research journals, which increases the worldwide availability of the results, and may aid researchers designing future studies. To allow for the results to be implemented in daily care, (inter)national BCC guidelines need to be adapted. OCT can be incorporated in the guideline as initial diagnostic strategy, omitting the need for a punch biopsy only if a BCC diagnosis can be made with high confidence. In cases where a BCC diagnosis cannot be made with high confidence, a biopsy is still needed.

Use of OCT will require re-organization of current clinical practice. In part of the patients (65.6%), in whom an OCT diagnosis can be made with high confidence, the clinical process will change from a punch biopsy with one to two weeks waiting time for the results, to a so-called one-stop-shop approach without the need for a punch biopsy. The first consultation will then partly change, because with OCT diagnosis and treatment are directly discussed with the patient. The proposed redesign of care is mostly an organizational change involving the de-implementation of routines (biopsy) and thereby adding new services (OCT). For that reason, it is essential that reimbursement becomes available for hospitals for the task of obtaining and interpreting OCT scans. Currently, no declaration can be performed for obtaining an OCT scan, whereas obtaining a punch biopsy is reimbursed. Consequently, it is important to involve the hospital financial department and health insurance companies. Another requirement for successful implementation of OCT in clinical practice is that users of OCT are well-trained. Therefore, it is essential to set criteria for adequate diagnostic performance and to quantify the time and training required to achieve a sufficient level of diagnostic performance.

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